09/881 326
AA #8

=> s vascula? or artery or arteriole or arteries or vein# or venous
L1 2668012 VASCULA? OR ARTERY OR ARTERIOLE OR ARTERIES OR VEIN# OR VENOUS

=> s parenchym

=> s dna or rna or plasmid# or polynucleotide# or (nucleic acid#) or oligonucleotide#
3 FILES SEARCHED...
L2 3410468 DNA OR RNA OR PLASMID# OR POLYNUCLEOTIDE# OR (NUCLEIC ACID#) OR OLIGONUCLEOTIDE#

=> s parenchym?

L3 112921 PARENCHYM?

=> s blood vessel#
L4 277514 BLOOD VESSEL#

=> s l1 or l4
L5 2774814 L1 OR L4

=> s l2 and l3 and l5
L6 1033 L2 AND L3 AND L5

=> s transfect? or transduc?
L7 813761 TRANSFECT? OR TRANSDUC?

=> s l2 and l3 and l5 and l7
L8 98 L2 AND L3 AND L5 AND L7

=> dup rem l8
PROCESSING COMPLETED FOR L8
L9 56 DUP REM L8 (42 DUPLICATES REMOVED)

=> s l9 and py<2000
1 FILES SEARCHED...
3 FILES SEARCHED...
4 FILES SEARCHED...
L10 31 L9 AND PY<2000

=> d l10 ibib abs 1-31

L10 ANSWER 1 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:325037 BIOSIS
DOCUMENT NUMBER: PREV199900325037
TITLE: Isolation of recombinant adeno-associated virus vector-cellular ***DNA*** junctions from mouse liver.
AUTHOR(S): Nakai, Hiroyuki (1); Iwaki, Yuichi; Kay, Mark A.; Couto, Linda B.
CORPORATE SOURCE: (1) Department of Pediatrics, Program in Human Gene Therapy, Stanford University School of Medicine, 300 Pasteur Dr., Stanford, CA, 94305 USA
SOURCE: Journal of Virology, (***July, 1999***) Vol. 73, No. 7, pp. 5438-5447.
ISSN: 0022-538X.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Recombinant adeno-associated virus (rAAV) vectors allow for sustained expression of transgene products from mouse liver following a single portal ***vein*** administration. Here a rAAV vector expressing human coagulation factor F.IX (hF.IX), AAV-EF1alpha-F.IX (hF.IX expression was controlled by the human elongation factor 1alpha (EF1alpha) enhancer-promoter) was injected into mice via the portal ***vein*** or tail ***vein*** , or directly into the liver ***parenchyma*** , and the forms of rAAV vector ***DNA*** extracted from the liver were analyzed. Southern blot analyses suggested that rAAV vector integrated into the host genome, forming mainly head-to-tail concatemers with occasional deletions of the inverted terminal repeats (ITRs) and their flanking sequences. To further confirm vector integration, we developed a shuttle vector system and isolated and sequenced rAAV vector-cellular ***DNA*** junctions from ***transduced*** mouse livers. Analysis of 18 junctions revealed various rearrangements, including ITR deletions and amplifications of the vector and cellular ***DNA*** sequences. The breakpoints of the vector were mostly located within the ITRs, and cellular ***DNA*** sequences were recombined with the vector genome in a nonhomologous manner. Two rAAV-targeted ***DNA*** sequences were identified as the mouse rRNA gene and the alpha1 collagen gene. These observations serve as direct evidence of rAAV integration into the host genome of mouse liver and allow us to begin to elucidate the mechanisms involved in rAAV integration into tissues in vivo.

L10 ANSWER 2 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:117004 BIOSIS
DOCUMENT NUMBER: PREV199900117004
TITLE: Intraarterial delivery of adenovirus vectors and liposome-***DNA*** complexes to experimental brain neoplasms.
AUTHOR(S): Rainov, Nikolai G.; Ikeda, Keiro; Qureshi, Nazir H.; Grover, Shivani; Herrlinger, Ulrich; Pechan, Peter; Chiocca, E. Antonio; Breakefield, Xandra O. (1); Barnett, Faith H.
CORPORATE SOURCE: (1) Massachusetts Gen. Hosp. East, Dep. Mol. Neurogenet., 13th St., Bldg. 149, 6th Floor, Charlestown, MA 02129 USA
SOURCE: Human Gene Therapy, (***Jan. 20, 1999***) Vol. 10, No. 2, pp. 311-318.
ISSN: 1043-0342.
DOCUMENT TYPE: Article
LANGUAGE: English
AB This study investigated the intraarterial delivery of genetically engineered replication-deficient adenovirus vectors (AVs) and cationic liposome- ***plasmid*** ***DNA*** complexes (lipoDNA) to experimental brain tumors. Adenovirus or lipoDNA was injected into the internal carotid ***artery*** (ICA) of F344 rats harboring intracerebral 9L gliosarcomas, using bradykinin (BK) to selectively permeabilize the blood-tumor barrier (BTB). Brain and internal organs of the animals were collected 48 hr after vector injection and stained for expression of the marker gene product, beta-galactosidase (beta-Gal). Intracarotid delivery of AV to 9L rat gliosarcoma without BTB disruption resulted in transgene expression in 3-10% of tumor cells distributed throughout the tumor. Virus-mediated expression of beta-gal gene products in this tumor model was particularly high in small foci (ltoreq 0.5 mm), which had invaded the normal brain tissue surrounding the main tumor mass. In these foci more than 50% of tumor cells were ***transduced*** . BK infusion increased the amount of transgene-expressing cells in larger tumor foci to 15-30%. In the brain ***parenchyma*** only a few endothelial cells expressed beta-gal owing to AV-mediated gene transfer. Intracarotid delivery of lipoDNA bearing a cytoplasmic expression cassette rendered more than 30% of the tumor cells positive for the marker gene without BTB disruption. The pattern of distribution was in general homogeneous throughout the tumor. BK infusion was able to increase further the number of ***transduced*** tumor cells to more than 50%. Although lipoDNA-mediated gene transfer showed increased efficacy as compared with AV-mediated gene transfer, it had less specificity since a larger number of endothelial and glial cells also expressed the transgene. AV and lipoDNA injections, in the absence and presence of BK, also resulted in ***transduction*** of peripheral organs. AV showed its known predilection for liver and lung. In the case of lipoDNA, ***parenchymal*** organs such as liver, lung, testes, lymphatic nodes, and especially spleen, were ***transduced*** . These findings indicate that intracarotid application of AV and lipoDNA vectors can effectively ***transduce*** tumor cells in the brain, and that BTB modulation by BK infusion can further increase the number of transgene-expressing tumor cells.

L10 ANSWER 3 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL

ABSTRACTS INC.
ACCESSION NUMBER: 1999:12089 BIOSIS
DOCUMENT NUMBER: PREV199900012089
TITLE: Expression of p53, p21 (Waf1/Cip1/Sdi1) and Fas antigen in collagen ***vascular*** and granulomatous lung diseases.
AUTHOR(S): Kunitake, R.; Kuwano, K. (1); Miyazaki, H.; Kawasaki, M.; Hagimoto, N.; Fujita, M.; Kaneko, Y.; Hara, N.
CORPORATE SOURCE: (1) Res. Inst. Dis. Chest, Fac. Med., Kyushu Univ., 3-1-1 Maidashi, Higashiku, Fukuoka 812-8582 Japan
SOURCE: European Respiratory Journal, (***Oct., 1998***) Vol. 12, No. 4, pp. 920-925. ISSN: 0903-1936.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Fas is expressed in various cells and ***transduces*** the cell death signal. p21 is a mediator of p53-dependent G1 arrest associated with deoxyribonucleic acid (***DNA***) damage. The upregulation of p53 and p21 associated with ***DNA*** damage in idiopathic pulmonary fibrosis has been described previously. In this study, p53, p21, and Fas expression and ***DNA*** damage were examined in interstitial pneumonia associated with collagen ***vascular*** diseases (CVD-IP). ***DNA*** damage was assessed by terminal deoxynucleotidyl transferase-mediated deoxyuridine triphosphate biotin nick end-labelling (TUNEL) and p53, p21 and Fas proteins were detected by immunohistochemistry in 13 cases of CVD-IP, 13 of sarcoidosis, seven of hypersensitivity pneumonitis (HP) and eight control patients with normal lung ***parenchyma*** . TUNEL-positive signals were found in bronchiolar or alveolar epithelial cells in 11 of 13 (85%) specimens of CVD-IP, but not in sarcoidosis, HP or controls, except for a case of chronic HP with pulmonary fibrosis. p53, p21 and Fas were detected in bronchiolar or alveolar epithelial cells in nine (69%), 10 (77%) and 12 (92%) of 13 specimens of CVD-IP, respectively, but not in sarcoidosis, HP or controls, except for a case of chronic HP. These results suggest that the upregulation of p53, p21 and Fas in bronchiolar and alveolar epithelial cells associated with deoxyribonucleic acid damage may participate in the process of pulmonary fibrosis in interstitial pneumonia associated with collagen ***vascular*** diseases and chronic hypersensitivity pneumonitis.

L10 ANSWER 4 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:493054 BIOSIS
DOCUMENT NUMBER: PREV199800493054
TITLE: Elastogenesis in the developing chick lung is transcriptionally regulated.
AUTHOR(S): James, Marianne F.; Rich, Celeste B.; Trinkaus-Randall, Vickery; Rosenbloom, Joel; Foster, Judith Ann
CORPORATE SOURCE: Dep. Biochem., Boston Univ. Sch. Med., 80 East Concord Street, Boston, MA 02118 USA
SOURCE: Developmental Dynamics, (***Oct., 1998***) Vol. 213, No. 2, pp. 170-181. ISSN: 1058-8388.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The overall goals of this study were to establish the level at which elastin gene expression is regulated during chick lung embryogenesis and to identify the temporal and spatial relationships among elastogenesis, smooth muscle cell differentiation, and cell proliferation. A comparison of lung elastin mRNA and transcriptional levels during embryogenesis shows that elastin expression is developmentally regulated at the transcriptional level. The increase in elastogenic activity occurs during the late stages of lung embryogenesis and coincides with terminal maturation of the tertiary bronchi. In situ hybridization analysis demonstrates that the increase in elastin mRNA expression is confined to the tertiary bronchial respiratory subunits, connective tissue septa, and supporting ***vasculature*** of the lung ***parenchyma*** . Immunohistochemical localization of smooth muscle cell alpha-actin and tropoelastin suggests that alpha-actin-immunoreactive cells of the lung ***parenchyma*** are a major contributor to the increase in elastin expression during embryogenesis. This observation is also reflected by Northern blot analysis, which demonstrates a temporal coincidence in the increase of both alpha-actin and elastin mRNA levels. Histone mRNA expression, which was used as an index of cellular proliferation, reveals a level and spatial pattern inversely related to that of the elastin transcript. Tissue ***transfections*** of chick lungs isolated from 18-day embryos with various elastin gene deletion/reporter constructs illustrate that the elastin promoter is not promiscuous within a tissue environment and that sequences spanning the -500 to +2 region are capable of directing promoter activity spatially comparable to the endogenous elastin gene.

L10 ANSWER 5 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1996:76109 BIOSIS
DOCUMENT NUMBER: PREV199698648244
TITLE: Receptor-mediated transfer of pSV2CAT ***DNA*** to mouse liver cells using asialofetuin-labeled liposomes.
AUTHOR(S): Hara, T.; Aramaki, Y.; Takada, S.; Koike, K.; Tsuchiya, S. (1)
CORPORATE SOURCE: (1) Dep. Biopharmaceutics, Sch. Pharmacy, Tokyo Univ. Pharmacy and Life Sci., 1432-1 Horinouchi, Hachioji, Tokyo 192-03 Japan
SOURCE: Gene Therapy, (1995) Vol. 2, No. 10, pp. 784-788. ISSN: 0969-7128.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Asialofetuin-labeled liposomes (AF-liposomes) were developed as a nonviral vector having high ***transfection*** activity for receptor-mediated gene transfer to hepatocytes by systemic administration. Initially, the majority of pSV2CAT, a chloramphenicol acetyltransferase (CAT) gene expression ***plasmid*** , was associated with AF-liposomes (AF-liposome-pSV2CAT), and they were injected into the portal ***vein*** of an adult mouse. Significantly high CAT activity was observed in the liver. The CAT activity in the liver was further increased two-fold by using AF-liposomes completely encapsulating pSV2CAT. Nonlabeled control liposomes, on the other hand, showed lower CAT activity in the liver than in the spleen or lung. The level of CAT mRNA reflected the CAT activity obtained by each liposome preparation in each tissue. Immunohistochemical staining showed that CAT was produced in a large number of ***parenchymal*** cells localizing in the periportal area. The ***plasmid*** encapsulated in the internal aqueous layer of the liposomes was effectively protected from environmental degradation. Thus, by administration into the blood circulation, AF-liposomes would be successfully incorporated into hepatocytes through receptor-mediated endocytosis, and the encapsulated ***plasmid*** would be transferred to the intracellular pathway.

L10 ANSWER 6 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1995:486607 BIOSIS
DOCUMENT NUMBER: PREV199598500907
TITLE: In Vivo ***Transfection*** of Hepatitis C Virus Complementary ***DNA*** Into Rodent Liver by Asialoglycoprotein Receptor Mediated Gene Delivery.
AUTHOR(S): Yamamoto, Masato; Hayashi, Norio (1); Miyamoto, Yasuhide; Takehara, Tetsuo; Mita, Eiji; Seki, Makoto; Fusamoto, Hideyuki; Kamada, Takenobu
CORPORATE SOURCE: (1) Dep. Med., Osaka Univ. Sch. Med., 2-2 Yamadaoka, Suita, Osaka 565 Japan
SOURCE: Hepatology, (1995) Vol. 22, No. 3, pp. 847-855. ISSN: 0270-9139.
DOCUMENT TYPE: Article
LANGUAGE: English
AB An in vivo model of hepatitis C virus (HCV) infection is needed to

enable
investigation of the mechanism of the liver injury that it causes. In this study, we used asialoglycoprotein receptor mediated gene delivery to obtain expression of the complementary ***DNA*** (cDNA) coding the
core and part of the envelope 1 protein of HCV because selective delivery to the hepatocytes has been reported to be attained with this method. The optimum carrier- ***DNA*** ratio was examined using in vitro ***transfection*** and found to be important for the efficiency of this method. In ***transfection*** in vivo, microautoradiographical examination showed that the ***transfected*** ***plasmids*** were delivered selectively to the liver ***parenchymal*** cells. To obtain an immunohistochemically detectable level of protein expression in rodent liver, some modifications for increasing the in vivo ***transfection*** efficiency were performed; a lysosomal enzyme inhibitor, chloroquine, was
used and the administration route of the carrier- ***DNA*** complex was
changed from the tail ***vein*** to the portal ***vein*** . On the bases of these results, in vivo ***transfection*** with expression vector of HCV core/E1 region was performed. In rat liver ***transfected*** by intraportal injection with chloroquine, the transcript ***RNA*** and the core protein were detected. These results indicated that the HCV core/E1 expression vector was not merely delivered
but also successfully expressed in the liver using asialoglycoprotein receptor mediated gene delivery. The number of the HCV core expressing cells in the ***transfected*** liver was similar to that in patients with hepatitis C. These in vivo ***transfected*** animals should be useful for investigating the role of this region in the liver injury caused by HCV.

L10 ANSWER 7 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1995:30984 BIOSIS
DOCUMENT NUMBER: PREV199598045284
TITLE: Catheter-mediated pulmonary ***vascular*** gene transfer and expression.
AUTHOR(S): Muller, David W. M. (1); Gordon, David; San, Hong; Yang,
Zhiyong; Pompili, Vincent J.; Nabel, Gary J.; Nabel, Elizabeth G.
CORPORATE SOURCE: (1) Univ. Mich. Med. Center, 9D, Room 9800, 1500 E Medical
Center, Dr., Ann Arbor, MI 48109-0022 USA
SOURCE: Circulation Research, (1994) Vol. 75, No. 6, pp. 1039-1049.
ISSN: 0009-7330.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The study and treatment of pulmonary diseases may be greatly facilitated
by in vivo expression of specific recombinant genes in the pulmonary ***vasculature*** and lung ***parenchyma*** . To evaluate the feasibility of gene transfer to the pulmonary ***vasculature*** , cationic liposomes and adenoviral vectors encoding a human placental alkaline phosphatase (hpAP) gene were delivered into a pulmonary ***artery*** of 24 pigs by percutaneous right heart catheterization. Pulmonary tissue was harvested within 20 minutes or 5, 14, or 28 days later and was analyzed for gone transfer and expression. Five days after exposure to liposomes or adenoviral vectors, transfer of ***DNA*** and
expression of mRNA were demonstrated in ***transfected*** lung tissue.
Recombinant alkaline phosphatase protein was observed in both the ***vasculature*** and in alveolar septa but not in the bronchi. Expression of hpAP protein was observed at 5 days, was diminished at 14 days, and was absent 28 days after gene transfer with both liposome and adenoviral vectors. No major adverse effects of gene expression were detected by histological examination of the ***transfected*** lung segments compared with control segments. Gene transfer to the lung by either vector was not associated with significant biochemical abnormalities or histological changes 5, 14, or 28 days later in other organs, including carotid ***artery*** , heart, liver, spleen, kidney, skeletal muscle, ovary, and testes. These studies demonstrate that after intravascular gene delivery to the lung, recombinant genes are expressed in the ***vasculature*** and alveoli. This approach may provide a useful model for the experimental study of pulmonary ***vascular*** diseases, including pulmonary fibrosis and pulmonary thrombosis disorders.

L10 ANSWER 8 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1994:443785 BIOSIS
DOCUMENT NUMBER: PREV199497456785
TITLE: Gene transfer into the mammalian kidney: Microtransplantation of retrovirus- ***transduced*** metanephric tissue.
AUTHOR(S): Woolf, Adrian S. (1); Bosch, Ricardo J.; Fine, Leon G.
CORPORATE SOURCE: (1) Dep. Med., University College Middlesex Sch. Med.,
Rayne Inst., 5 University St., London WC1E 6JJ UK
SOURCE: Experimental Nephrology, (1993) Vol. 1, No. 1, pp. 41-48.
ISSN: 1018-7782.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Our previous observation that embryonic kidney tissue can develop and differentiate when transplanted into the ***parenchyma*** of mouse kidneys in the postnatal period provided an avenue for transferring novel genes into the mammalian kidney in vivo. Mouse metanephric tissue was infected ex vivo with a replication defective retrovirus which ***transduces*** the gene for beta-galactosidase. Seven to 21 days after
transplantation of this tissue into neonatal and adult mouse kidneys, the expression of the gene, controlled by the viral long-terminal repeat promoter, was noted in approximately one-third of implants. Gene expression occurred predominantly in glomerular epithelial cells, but also in interstitial cells and in ***vascular*** structures. Polymerase chain reaction amplification of renal genomic ***DNA*** indicated the presence of viral ***DNA*** in 9 of 10 kidneys which had received metanephric implants into the neonatal renal cortex. These studies demonstrate the feasibility of short-term gene transfer into and expression within the mammalian kidney.

L10 ANSWER 9 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1993:387940 BIOSIS
DOCUMENT NUMBER: PREV199396063240
TITLE: Systemic gene expression after intravenous ***DNA*** delivery into adult mice.
AUTHOR(S): Zhu, Ning; Liggitt, Denny; Liu, Yong; Debs, Robert (1)
CORPORATE SOURCE: (1) Cancer Res. Inst., Univ. Calif., San Francisco, CA
94143-0128 USA
SOURCE: Science (Washington D C), (1993) Vol. 261, No. 5118, pp.
209-211.
ISSN: 0036-8075.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Direct gene transfer into adult animals resulting in generalized or tissue-specific expression would facilitate rapid analysis of transgene effects and allow precise in vivo manipulation of biologic processes at the molecular level. A single intravenous injection of expression ***plasmid*** :cationic liposome complexes into adult mice efficiently ***transfected*** virtually all tissues. In addition to ***vascular*** endothelial cells, most of the extravascular ***parenchymal*** cells present in many tissues including the lung, spleen, lymph nodes, and bone marrow expressed the transgene without any apparent treatment-related toxicity. The transgene was still expressed in large numbers of cells in multiple tissues for at least 9 weeks after a single injection. Expression could be targeted to specific tissues and cell types, depending on the promoter element used.

L10 ANSWER 10 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1993:144001 BIOSIS
DOCUMENT NUMBER: PREV199395076801
TITLE: Cell surface extensions associated with overexpression of Alzheimer beta/A4 amyloid.
AUTHOR(S): Maestre, Gladys E.; Tate, Barbara; Majocha, Ronald E.; Marotta, Charles A. (1)
CORPORATE SOURCE: (1) Dep. Psychiatry Human Behav., Brown Univ., Miriam
Hosp., 164 Summit Ave., Providence, Rhode Island 02906 USA

SOURCE: Brain Research, (1992) Vol. 599, No. 1, pp. 64-72.
ISSN: 0006-8993.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Deposition of beta/A4 amyloid in Alzheimer disease (AD) brain ***parenchyma*** and ***vasculature*** occurs by mechanisms that are currently undefined. Similarly the potential consequences of amyloid accumulation for disrupting cellular integrity have not been addressed in detail. To investigate the possible significance of amyloid deposits for cellular viability, PC12 cells were permanently ***transfected*** with ***DNA*** coding for the beta/A4-C terminal region of the amyloid precursor protein. The ***DNA*** represented 97 amino acids of the amyloid precursor protein of which 40 amino acids were derived from the beta/A4 region. ***Transfected*** clonal cell lines and controls were examined at both the light and electron microscopic levels for morphological abnormalities. beta/A4 amyloid accumulated in the cell membrane where the peptide was located at cellular processes resembling blebs and microvilli. These specialized structures at the cell surface were over-abundant in ***transfected*** cells that overexpressed the beta/A4 peptide but not in controls. Membranous processes may be involved in the delivery of the beta/A4 peptide to the external surface of the cell of origin and release into the extracellular space. Similar surface features of cells in the AD brain, should they occur, may indicate a role for membrane-associated processes in the pathophysiology of the disorder.

L10 ANSWER 11 OF 31 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999160027 EMBASE
TITLE: After portal branch ligation in rat, nuclear factor .kappa.B, interleukin-6, signal ***transducers*** and activators of transcription 3, c-fos, c-myc, and c- jun are similarly induced in the ligated and nonligated lobes.
AUTHOR: Starkel P.; Horsmans Y.; Sempoux C.; De Saeger C.; Wary J.; Lause P.; Maiter D.; Lambotte L.
CORPORATE SOURCE: Dr. Y. Horsmans, Department of Gastroenterology, St. Luc University Hospital, Av. Hippocrate 10, 1200 Brussels, Belgium. Horsmans@gaen.ucl.ac.be
SOURCE: Hepatology, (1999) 29/5 (1463-1470).
Refs: 31
ISSN: 0270-9139 CODEN: HPTLD
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 022 Human Genetics
029 Clinical Biochemistry
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Several studies have emphasized the involvement of transcription factors, cytokines, and proto-oncogenes in initiating the regenerative process after partial hepatectomy. To assess whether these events do specifically occur in a cellular system undergoing regeneration, we studied the induction of nuclear factor .kappa.B (NF.kappa.B), interleukin-6 (IL-6), signal ***transducers*** and activators of transcription 3 (Stat3), c-fos, c-myc, c-jun, after portal branch ligation (PBL), which produces atrophy of the deprived lobes (70% of the liver ***parenchyma***), whereas the perfused lobes undergo compensatory regeneration. Nuclear extracts and total ***RNA*** were prepared from control livers as well as from atrophying and regenerating lobes at 0.5, 1, 2, 5, and 8 after PBL NF.kappa.B and Stat3 induction were studied by electrophoretic mobility shift assays and Western blotting. IL-6 and proto- oncogenes expressions were assessed by reverse transcription polymerase chain reaction and Northern blotting, respectively. Assays were also performed after a sham operation. NF.kappa.B and Stat3 protein expression and ***DNA*** binding were rapidly and similarly induced in nuclear extracts from the atrophying and regenerating lobes. IL-6 was elevated in both lobes from 1 to 8 hours after PBL as well as c-fos, c-myc, and c-Jun during the first 2 hours. IL-6 and Stat3 but not NF.kappa.B were also elevated after a sham operation. These findings suggest that the cellular and molecular changes occurring early in a regenerating liver are nonspecific, possibly stress-induced, cellular responses. They do not indicate the future evolution towards atrophy or regeneration.

L10 ANSWER 12 OF 31 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97122621 EMBASE
DOCUMENT NUMBER: 1997122621
TITLE: Adenovirus-mediated gene transfer using in-situ perfusion of the liver graft.
AUTHOR: Shiraishi M.; Kusano T.; Hara J.; Hiroyasu S.; Shao-ping M.; Makino Y.; Muto Y.
CORPORATE SOURCE: M. Shiraishi, The First Department of Surgery, University of Ryukyu, School of Medicine, Uehara 207, Nishihara-cho, Okinawa 903-01, Japan
SOURCE: Transplant International, (1997) 10/3 (202-206).
Refs: 15
ISSN: 0934-0874 CODEN: TRINE5
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 009 Surgery
022 Human Genetics
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB To establish an efficient technique for adenovirus-mediated gene transfer in liver transplantation, we evaluated the in situ perfusion of liver grafts. The grafts were perfused in situ with 1 x 1010 of E1-deleted, replication-defective aden oviral vectors encoding the LacZ gene driven by the human CMV promoter, either through the hepatic ***artery*** (group 1) or the portal ***vein*** (group 2). Group 3 animals served as negative controls; their liver grafts were perfused with lactated Ringer's solution through the portal ***vein*** . PCR confirmed the presence of viral ***DNA*** in every graft perfused with viral vectors. In X-gal staining, positive staining was observed almost exclusively at the portal triad in group 1, whereas in group 2 minimal staining was observed, predominantly in the ***parenchymal*** area. Protein production from the ***transfected*** gene was confirmed by a functional protein assay; the values were 0.16% .+-. 0.07% liver protein in group 1, 0.13% .+-. 0.02% in group 2, and 0.007% .+-. 0.0003% in group 3 on postoperative day 2. In conclusion, in situ perfusion of the viral vectors through the hepatic ***artery*** resulted in an effective expression of the ***transfected*** gene, predominantly at the portal triad.

L10 ANSWER 13 OF 31 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 94303245 EMBASE
DOCUMENT NUMBER: 1994303245
TITLE: Cellular localization of vasopressin V1a receptor messenger ribonucleic acid in adult male rat brain, pineal, and brain ***vasculature*** .
AUTHOR: Ostrowski N.L.; Lolait S.J.; Young III W.S.
CORPORATE SOURCE: Laboratory of Cell Biology, National Institute of Mental Health, National Institutes of Health,Bethesda, MD 20892, United States
SOURCE: Endocrinology, (1994) 135/4 (1511-1528).
ISSN: 0013-7227 CODEN: ENDOAO
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Vasopressin V1a receptor (V1aR) transcripts were localized in brain, pineal, and superficial brain ***vascular*** tissues of adult male rats using hybridization histochemistry and an [35S]riboprobe complementary to the messenger ribonucleic acid (mRNA) encoding the fifth to the midseventh transmembrane regions of the receptor. V1aR mRNA was extensively distributed throughout brain and was expressed in 1) superficial cells of the granule cell layers of the main olfactory bulb, hippocampal dentate gyrus, and cerebellum; 2) numerous anatomically distinct brain nuclei; 3) isolated cells dispersed throughout the central nervous system; 4) cells of the choroid plexus, occasional ***blood*** ***vessels*** in the olfactory bulb and interpeduncular nucleus, and extraparenchymal intracranial ***vasculature*** ; and 5) some white

matter structures. Numerous cells expressing V1aR transcripts were found in forebrain structures, including primary olfactory (piriform) cortex, the anterior and posterior olfactory nuclei; dorsal, intermediate, and ventral lateral septal nuclei; the septo-fimbrial nucleus and accumbens nucleus; and numerous hypothalamic regions with the most intense hypothalamic labeling in the arcuate, stigmoid, suprachiasmatic, and periventricular nuclei and the lateral hypothalamic area. Cells expressing V1aR transcripts were ubiquitous throughout the midbrain, pontine, and medullary regions. A lower intensity signal was found in cells of the parvocellular paraventricular and anteroventral nucleus of the thalamus, circumventricular organs including the pineal, and the subfornical organ. V1aR transcripts were not generally detected in ***parenchymal*** ***vasculature*** , but could be found over large ***blood*** ***vessels*** in the interpeduncular nucleus and medial olfactory bulb; transcripts were commonly detected in perivascular brain cells. V1aR mRNA
was abundantly expressed by choroid plexus, endothelial cells of midline ***blood*** ***vessels*** between the main olfactory bulbs, and superficial ***vascular*** tissue on all brain surfaces. These data confirm the presence of the ***vascular*** /hepatic-type V1aR gene in brain tissue and document an extensive expression. The distribution of V1aR mRNA suggests that there are at least two types of vasopressin-responsive cells in brain: one type exemplified by lateral septal area neurons innervated by classical axodendritic/somatic synaptic vasopressinergic terminals and a second, perivascular/ ***vascular*** type that would facilitate humoral vasopressinergic signaling in the brain.

L10 ANSWER 14 OF 31 MEDLINE
ACCESSION NUMBER: 1999438393 MEDLINE
DOCUMENT NUMBER: 99438393 PubMed ID: 10508515
TITLE: Truncating mutations in CCM1, encoding KRIT1, cause hereditary cavernous angiomas.
AUTHOR: Laberge-le Couteulx S; Jung H H; Labauge P; Houtteville J
P; Lescoat C; Cecillon M; Marechal E; Joutel A; Bach J F; Tournier-Lasserve E
CORPORATE SOURCE: INSERM U25, Faculte de Medecine Necker, 156 Rue de
Vaugirard, 75730 Paris Cedex 15, France.
SOURCE: NATURE GENETICS, ***(1999 Oct)*** 23 (2) 189-93.
Journal code: 9216904. ISSN: 1061-4036.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199910
ENTRY DATE: Entered STN: 19991101
Last Updated on STN: 19991101
Entered Medline: 19991019
AB Cavernous angiomas are ***vascular*** malformations mostly located in
the central nervous system and characterized by enlarged capillary cavities without intervening brain ***parenchyma*** . Clinical symptoms
include seizures, haemorrhage and focal neurological deficits. Cavernous angiomas prevalence is close to 0.5% in the general population. They may be inherited as an autosomal dominant condition in as much as 50% of cases. Cerebral cavernous malformations (CCM) loci were previously identified on 7q, 7p and 3q (refs 4,5). A strong founder effect was observed in the Hispano-American population, all families being linked to CCM1 on 7q (refs 4,7). CCM1 locus assignment was refined to a 4-cM interval bracketed by D7S2410 and D7S689 (ref. 8). Here we report a physical and transcriptional map of this interval and that CCM1, a gene whose protein product, KRIT1, interacts with RAP1A (also known as KREV1;
ref. 9), a member of the RAS family of GTPases, is mutated in CCM1 families. Our data suggest the involvement of the RAP1A signal ***transduction*** pathway in vasculogenesis or angiogenesis.

L10 ANSWER 15 OF 31 MEDLINE
ACCESSION NUMBER: 1999217046 MEDLINE
DOCUMENT NUMBER: 99217046 PubMed ID: 10200989
TITLE: Hypoxia-induced adrenomedullin production in the kidney.
AUTHOR: Nagata D; Hirata Y; Suzuki E; Kakoki M; Hayakawa H; Goto A;
Ishimitsu T; Minamino N; Ono Y; Kangawa K; Matsuo H; Omata
M
CORPORATE SOURCE: Second Department of Internal Medicine, Faculty of
Medicine, University of Tokyo, Japan.
SOURCE: KIDNEY INTERNATIONAL, ***(1999 Apr)*** 55 (4) 1259-67.
Journal code: 0323470. ISSN: 0085-2538.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U96127
ENTRY MONTH: 199907
ENTRY DATE: Entered STN: 19990727
Last Updated on STN: 19990727
Entered Medline: 19990714
AB BACKGROUND: Adrenomedullin (AM) is a newly discovered peptide that has a
potent vasorelaxant activity. To investigate its potential roles in hypoxia-induced renal injury, we examined whether AM production in the kidney increased under hypoxic conditions. METHODS: The AM transcript
levels in Madin-Darby canine kidney (MDCK) cells, rat ***vascular*** smooth muscle cells (VSMCs), and rat mesangial cells were assessed by Northern blot analyses under normoxic and hypoxic conditions. The AM peptide in culture media was measured by radioimmunoassay. The effects of
hypoxia on accumulation of cAMP in VSMCs were also examined. The stability
of AM transcripts under normoxic and hypoxic conditions was compared in
the presence of actinomycin D. The effects of hypoxia on AM promoter activity was assessed by transient ***transfection*** assays using the AM promoter subcloned upstream of luciferase gene. RESULTS: The expression
of AM transcripts increased significantly in MDCK cells, rat VSMCs, and rat mesangial cells under hypoxic conditions without changes in the stability of AM transcripts; however, the AM promoter activity under hypoxic was not elevated significantly. The accumulation of AM peptide in
culture media also increased significantly under hypoxic conditions in MDCK cells (2.2 +/- 0.1 fmol/10(5) cells in normoxia vs. 3.5 +/- 0.3 fmol/10(5) cells in hypoxia, 6 hr after hypoxia induction, $P < 0.001$), and in rat VSMCs (5.5 +/- 0.3 fmol/10(5) cells in normoxia vs. 7.8 +/- 0.4 fmol/10(5) cells in hypoxia, 8 hr after hypoxia induction, $P < 0.01$). Under hypoxic conditions, cAMP levels in rat VSMCs increased significantly
compared with those under normoxic conditions (13.3 +/- 1.4 pmol/well vs.
4.6 +/- 0.4 pmol/well, $P < 0.01$). CONCLUSIONS: Renal ***parenchymal***
cells as well as renal vessels may produce AM under hypoxic conditions.

L10 ANSWER 16 OF 31 MEDLINE
ACCESSION NUMBER: 1999077469 MEDLINE
DOCUMENT NUMBER: 99077469 PubMed ID: 9862633
TITLE: SPARC: a signal of astrocytic neoplastic transformation and reactive response in human primary and xenograft gliomas.
AUTHOR: Rempel S A; Golembieski W A; Ge S; Lemke N; Elisevich K;
Mikkelsen T; Gutierrez J A
CORPORATE SOURCE: Henry Ford Midwest Neuro-Oncology Center and the Department
of Neurosurgery, Henry Ford Health Sciences Center, Detroit, Michigan 48202, USA.
SOURCE: JOURNAL OF NEUROPATHOLOGY AND EXPERIMENTAL NEUROLOGY,
(1998 Dec) 57 (12) 1112-21.
Journal code: 2985192R. ISSN: 0022-3069.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199901
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19990107

AB In an attempt to identify genetic alterations occurring early in astrocytoma progression, we performed subtractive hybridization between astrocytoma and glioblastoma cDNA libraries. We identified secreted protein acidic and rich in cysteine (SPARC), a protein implicated in cell-matrix interactions, as a gene overexpressed early in progression. Northern blot and immunohistochemical analyses indicated that transcript and protein were both elevated in all tumor specimens (grades II-IV) examined when compared with levels in normal brain. The level of SPARC expression was found to be tumor-dependent rather than grade-related. Immunohistochemically, SPARC protein was found to be overexpressed in 1) cells in the less cellularly dense regions within the tumor mass, 2) histomorphologically neoplastic-looking cells in adjacent normal brain at the tumor/brain interface, 3) neovessel endothelial cells in both the tumor and adjacent normal brain, and 4) reactive astrocytes in normal brain adjacent to tumor. Using a combination of ***DNA*** in situ hybridization and protein immunohistochemical analyses of the human/rat xenograft, SPARC expression was observed in the human glioma cells within the tumor mass, and in cells that invaded along ***vascular*** basement membranes and individually into the rat brain ***parenchyma*** , suggesting it may be an invasion-related gene. While it remains to be determined whether SPARC functionally contributes to tumor cell invasion, these data suggest that the early onset of increased SPARC expression, though complex, may serve as a signal indicative of neoplastic astrocytic transformation and reactive response to tumor-induced stress.

L10 ANSWER 17 OF 31 MEDLINE
ACCESSION NUMBER: 1999006492 MEDLINE
DOCUMENT NUMBER: 99006492 PubMed ID: 9792028
TITLE: The mechanisms of hepatic sinusoidal endothelial cell regeneration: a possible communication system associated with ***vascular*** endothelial growth factor in liver cells.
AUTHOR: Mochida S; Ishikawa K; Toshima K; Inao M; Ikeda H; Matsui A; Shibuya M; Fujiwara K
CORPORATE SOURCE: Third Department of Internal Medicine, Saitama Medical School, Japan.. smochida@saitama-med.ac.jp
SOURCE: JOURNAL OF GASTROENTEROLOGY AND HEPATOLOGY, ***(1998*** *** Sep)*** 13 Suppl S1-5.
Journal code: 8607909. ISSN: 0815-9319.
PUB. COUNTRY: Australia
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199901
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 20000303
Entered Medline: 19990105
AB ***Vascular*** endothelial growth factor (VEGF) has been shown to induce proliferation of sinusoidal endothelial cells in primary culture. To elucidate the mechanisms of sinusoidal endothelial cell regeneration in vivo, mRNA expression of VEGF and its receptors, flt-1 and KDR/flk-1, were studied in rat livers. Northern blot analysis revealed that VEGF-mRNA was expressed in hepatocytes immediately after isolation from normal rats. In contrast, non- ***parenchymal*** cells, including sinusoidal endothelial cells, expressed VEGF receptor-mRNA. ***Vascular*** endothelial growth factor-mRNA expression in hepatocytes was decreased during primary culture, but increased following a peak of ***DNA*** synthesis, induced by addition of epidermal growth factor or hepatocyte growth factor to the culture medium at 24 h of plating. In a 70% resected rat liver, VEGF-mRNA expression increased with a peak at 72 h after the operation, and mRNA expression of VEGF receptors between 72 and 168 h. In such a liver, mitosis was maximal in hepatocytes at 36 h and in sinusoidal endothelial cells at 96 h. Also, mRNA expression of both VEGF and its receptors was significantly increased in carbon tetrachloride-intoxicated rat liver compared with normal rat liver. ***Vascular*** endothelial growth factor expression was minimal in Kupffer cells isolated from normal rats, but marked in activated Kupffer cells and hepatic macrophages from the intoxicated rats. ***Vascular*** endothelial growth factor-mRNA expression was also increased in activated stellate cells from these rats and in the cells activated during primary culture compared with quiescent cells. We conclude that increased levels of VEGF expression in regenerating hepatocytes may contribute to the proliferation of sinusoidal endothelial cells in partially resected rat liver, probably through VEGF receptors up-regulated on the cells. Also, VEGF derived from activated Kupffer cells, hepatic macrophages and stellate cells may be involved in this proliferation in injured rat liver.

L10 ANSWER 18 OF 31 MEDLINE
ACCESSION NUMBER: 1998299937 MEDLINE
DOCUMENT NUMBER: 98299937 PubMed ID: 9636308
TITLE: Expression of the rabies virus glycoprotein in transgenic tomatoes.
AUTHOR: McGarvey P B; Hammond J; Dienelt M M; Hooper D C; Fu Z F; Dietzschold B; Koprowski H; Michaels F H
CORPORATE SOURCE: Thomas Jefferson University, Department of Microbiology and Immunology, Philadelphia, PA 19107, USA.. pmcgarve@lac.jci.tju.edu
SOURCE: BIO/TECHNOLOGY, ***(1995 Dec)*** 13 (13) 1484-7.
Journal code: 8309273. ISSN: 0733-222X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Biotechnology
ENTRY MONTH: 199807
ENTRY DATE: Entered STN: 19980731
Last Updated on STN: 19980731
Entered Medline: 19980721
AB We have engineered tomato plants (Lycopersicon esculentum Mill var. UC82b) to express a gene for the glycoprotein (G-protein), which coats the outer surface of the rabies virus. The recombinant constructs contained the G-protein gene from the ERA strain of rabies virus, including the signal peptide, under the control of the 35S promoter of cauliflower mosaic virus. Plants were transformed by Agrobacterium tumefaciens-mediated transformation of cotyledons and tissue culture on selective media. PCR confirmed the presence of the G-protein gene in plants surviving selection. Northern blot analysis indicated that ***RNA*** of the appropriate molecular weight was produced in both leaves and fruit of the transgenic plants. The recombinant G-protein was immunoprecipitated and detected by Western blot from leaves and fruit using different antisera. The G-protein expressed in tomato appeared as two distinct bands with apparent molecular mass of 62 and 60 kDa as compared to the 66 kDa observed for G-protein from virus grown in BHK cells. Electron microscopy of leaf tissue using immunogold-labeling and antisera specific for rabies G-protein showed localization of the G-protein to the Golgi bodies, vesicles, plasmalemma and cell walls of ***vascular*** ***parenchyma*** cells. In light of our previous demonstration that orally administered rabies G-protein from the same ERA strain elicits protective immunity in animals, these transgenic plants should provide a valuable tool for the development of edible oral vaccines.

L10 ANSWER 19 OF 31 MEDLINE
ACCESSION NUMBER: 96415739 MEDLINE
DOCUMENT NUMBER: 96415739 PubMed ID: 8818646
TITLE: Naked ***DNA*** delivered intraportally expresses efficiently in hepatocytes.
AUTHOR: Budker V; Zhang G; Knechtle S; Wolff J A
CORPORATE SOURCE: Department of Pediatrics, Waisman Center, University of Wisconsin-Madison 53705, USA.
SOURCE: GENE THERAPY, ***(1996 Jul)*** 3 (7) 593-8.
Journal code: 9421525. ISSN: 0969-7128.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 20000303
Entered Medline: 19961203

AB Naked ***plasmid*** ***DNA*** in hypertonic solutions was injected
intraportally in mice whose hepatic ***veins*** were transiently occluded. High levels of luciferase expression and beta-galactosidase expression in 1% of the hepatocytes throughout the entire liver were achieved using 100 micrograms of the respective ***plasmid*** vector. Two days after the intraportal injection of 100 micrograms of pCMVGH, the
mean hGH serum concentration was 65 ng/ml +/- 26 (n = 7) which is approximately 50-fold above normal baseline levels. These unprecedented levels of foreign gene expression from naked ***plasmid*** ***DNA***
document the ability of ***parenchymal*** cells in vivo to take up naked ***DNA*** following intravascular delivery.

L10 ANSWER 20 OF 31 MEDLINE
ACCESSION NUMBER: 96115616 MEDLINE
DOCUMENT NUMBER: 96115616 PubMed ID: 8679246
TITLE: Basic fibroblast growth factor alterations during development of monocrotaline-induced pulmonary hypertension in rats.
AUTHOR: Arcot S S; Fagerland J A; Lipke D W; Gillespie M N; Olson J
W
CORPORATE SOURCE: Division of Pharmacology and Experimental Therapeutics,
College of Pharmacy, University of Kentucky, Lexington 40536-0082, USA.
CONTRACT NUMBER: HL36404 (NHLBI)
HL38475 (NHLBI)
HL44084 (NHLBI)
+
SOURCE: GROWTH FACTORS, ***(1995)*** 12 (2) 121-30.
Journal code: 9000468. ISSN: 0897-7194.
PUB. COUNTRY: Switzerland
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199608
ENTRY DATE: Entered STN: 19960828
Last Updated on STN: 19970203
Entered Medline: 19960821
AB The chemical signaling pathways which orchestrate lung cell responses in
hypertensive pulmonary ***vascular*** disease are poorly understood. The present study examined temporal alterations in lung basic Fibroblast Growth Factor (bFGF) in a well characterized rat model of monocrotaline (MCT)-induced pulmonary hypertension. By immunohistochemical analysis,
there were progressive increases in bFGF in airway, ***vascular*** and
gas exchange regions of MCT-treated rat lungs. Increases in bFGF preceded
the onset of right ventricular hypertrophy at day 21 after MCT administration. Enhanced bFGF immunostaining was observed as early as day
4 in focal areas of the ***parenchyma*** , and by day 14 there was enhanced bFGF staining in alveolar macrophages, neutrophils and alveolar septa, which persisted through day 21. In conducting airways, there was elevated bFGF immunostaining in the smooth muscle cell (SMC) layer by days
4 and 7 and in the ciliated epithelium and its basement membrane at days 14 and 21. Cells morphologically similar to Clara cells in the luminal surfaces of bronchioles stained intensely on days 14 and 21. In the nucleus and cytoplasm of medial SMCs within pulmonary ***arteries*** ,
there was a progressive increase in bFGF staining starting at day 4. Lung bFGF mRNA was increased slightly at days 1, 4 and 7, while lung bFGF protein, as judged by western blot analysis, was increased at days 14 and 21 compared to controls. The present results, considered in teh light of teh documented roles of bFGF in ***vascular*** cell migration, growth and synthesis of extracellular matrix components, suggest that bFGF may contribute to the structural remodeling processes underlying the development of chronic pulmonary hypertension in MCT-treated rats.

L10 ANSWER 21 OF 31 MEDLINE
ACCESSION NUMBER: 95310852 MEDLINE
DOCUMENT NUMBER: 95310852 PubMed ID: 7540650
TITLE: N-formylpeptide and complement C5a receptors are expressed
in liver cells and mediate hepatic acute phase gene regulation.
AUTHOR: McCoy R; Haviland D L; Molmenti E P; Ziambaras T; Wetsel R
A; Perlmutter D H
CORPORATE SOURCE: Department of Pediatrics, Washington University School of
Medicine, St. Louis, Missouri 63110, USA.
CONTRACT NUMBER: AI00919 (NIAID)
AI25011 (NIAID)
HL37784 (NHLBI)
SOURCE: JOURNAL OF EXPERIMENTAL MEDICINE, ***(1995 Jul 1)***
182 (1) 207-17.
Journal code: 2985109R. ISSN: 0022-1007.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199507
ENTRY DATE: Entered STN: 19950807
Last Updated on STN: 20000303
Entered Medline: 19950725
AB Although the classical chemotactic receptor for complement anaphylatoxin
C5a has been associated with polymorphonuclear and mononuclear phagocytes,
several recent studies have indicated that this receptor is expressed on nonmyeloid cells including human endothelial cells, ***vascular*** smooth muscle cells, bronchial and alveolar epithelial cells, hepatocytes, and in the human hepatoma cell line HepG2. In this study, we examined the
possibility that other members of the chemotactic receptor family are expressed in HepG2 cells and human liver, and the possibility that such receptors mediate changes in acute phase gene expression in HepG2 cells. Using polymerase chain reaction (PCR) amplification of HepG2 mRNA with
primers based on highly conserved regions of the chemotactic subgroup of the G protein-coupled receptor family, we identified a PCR fragment from the formyl-methionyl-leucyl-phenylalanine (FMLP) receptor, as well as one
from the C5a receptor. Immunostaining with antipeptide antisera to FMLPR
confirmed the presence of this receptor in HepG2 cells. Receptor binding studies showed specific saturable binding of a radioiodinated FMLP analogue to HepG2 cells (Kd approximately 2.47 nM; R approximately 6 x
10(3) plasma membrane receptors per cell). In situ hybridization analysis showed the presence of FMLPR mRNA in ***parenchymal*** cells of the
human liver in vivo. Both C5a and FMLP mediated concentration- and time-dependent changes in synthesis of acute phase proteins in HepG2 cells
including increases in complement C3, factor B, and alpha 1-antichymotrypsin, as well as concomitant decreases in albumin and transferrin synthesis. The effects of C5a and FMLP on the synthesis of these acute phase proteins was evident at concentrations as low as 1 nM, and they were specifically blocked by antipeptide antisera for the corresponding receptor. In contrast to the effect of other mediators of hepatic acute phase gene regulation, such as interleukin 6, the effects of C5a and FMLP were reversed by increased concentrations well above the saturation point of the respective receptor. These results suggest that acute phase gene regulation by C5a and FMLP is desensitized at high concentrations, a property that is unique among the several known mechanisms for hepatic acute phase gene regulation.

L10 ANSWER 22 OF 31 MEDLINE
ACCESSION NUMBER: 94124188 MEDLINE
DOCUMENT NUMBER: 94124188 PubMed ID: 7507467
TITLE: Early and rapid de novo synthesis of Alzheimer beta A4-amyloid precursor protein (APP) in activated microglia.
AUTHOR: Banati R B; Gehrmann J; Czech C; Monning U; Jones L L;
Konig G; Beyreuther K; Kreutzberg G W
CORPORATE SOURCE: Department of Neuromorphology, Max-Planck-Institute of

Psychiatry, Martinsried, Germany.
SOURCE: GLIA, ***(1993 Nov)*** 9 (3) 199-210.
Journal code: 8806785. ISSN: 0894-1491.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199402
ENTRY DATE: Entered STN: 19940314
Last Updated on STN: 19960129
Entered Medline: 19940228
AB Upon acute activation, microglia, the immuneffector cells of the brain ***parenchyma*** , express the amyloid precursor protein (APP) that is otherwise prominent in pathological structures related to Alzheimer's disease. In this disease complex amyloid-bearing neuritic plaques contain beta A4-amyloid protein, the APP, and numerous inflammatory proteins. The accompanying activation of microglia has mostly been viewed as a secondary reaction to amyloid deposits. Activation of microglia was performed in a graded fashion. Transection of peripheral nerves such as the facial or sciatic nerve causes a microglial reaction within hours in the nucleus of origin or in projection areas of the CNS. A predominantly glial up-regulation of APP mRNA and protein could be detected as early as 6 h post lesion not only at the site of affected neuronal cell bodies but also in corresponding projection areas. Its time course suggests rapid transneuronal signalling to glial cells in the projection area. Light and electron microscopy demonstrate that microglia, which are cells of mononuclear phagocyte lineage and comprise up to 20% of all glial cells, are the dominant source for non-neuronal APP expression. Ultrastructurally, brain perivascular cells within the basal lamina constitutively express APP and thus are a possible source of ***vascular*** amyloid. Additionally, microglia express leukocyte-derived (L)-APP mRNA and protein that have recently been described in mononuclear cells of the immune system. Increased L-APP expression may serve as a potential marker for glial/microglial activation. Such immune-mediated amyloidogenesis initiated by microglia might have implications for the treatment of neurodegenerative diseases.

L10 ANSWER 23 OF 31 MEDLINE
ACCESSION NUMBER: 93129663 MEDLINE
DOCUMENT NUMBER: 93129663 PubMed ID: 1482704
TITLE: Hepatic gene therapy: persistent expression of human alpha 1-antitrypsin in mice after direct gene delivery in vivo.
AUTHOR: Kay M A; Li Q; Liu T J; Leland F; Toman C; Finegold M; Woo S L
CORPORATE SOURCE: Department of Cell Biology, Baylor College of Medicine, Houston, TX 77030.
CONTRACT NUMBER: DK-40162 (NIDDK)
DK-44080 (NIDDK)
GM13894 (NIGMS)
SOURCE: HUMAN GENE THERAPY, ***(1992 Dec)*** 3 (6) 641-7.
Journal code: 9008950. ISSN: 1043-0342.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199302
ENTRY DATE: Entered STN: 19930226
Last Updated on STN: 19930226
Entered Medline: 19930218
AB The liver represents an excellent target organ for gene therapy. The current strategy for hepatic gene therapy involves the isolation of primary hepatocytes from a resected liver lobe, ***transduction*** of therapeutic genes in vitro followed by autologous hepatocellular transplantation. This ex vivo approach is a rather complex procedure in its entirety; thus, a simple method for direct gene delivery into hepatocytes in vivo has been developed. The procedure involves partial hepatectomy followed by the portal ***vein*** infusion of recombinant retroviral vectors. Histological analysis of hepatocytes after in vivo delivery of a recombinant retrovirus bearing the E. coli beta-galactosidase gene showed that 1-2% of the ***parenchymal*** cells were ***transduced*** . Direct hepatic transfer of human alpha 1-antitrypsin cDNA under the transcriptional direction of the albumin promoter-enhancer led to constitutive expression of the human protein in the sera of recipients at concentrations of 30-1,400 ng/ml for at least 6 months. The experimental animals showed no signs of illness and histologic analysis of the liver revealed no evidence of pathologic abnormalities. The results suggest that the in vivo approach is an attractive alternative for hepatic gene therapy.

L10 ANSWER 24 OF 31 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2000-062007 [05] WPIDS
DOC. NO. CPI: C2000-017123
TITLE: Delivering ***polynucleotides*** into ***parenchymal*** cells useful e.g. in gene therapy.
DERWENT CLASS: B04 D16
INVENTOR(S): BUDKER, V G; KNECHTLE, S J; WOLFF, J A
PATENT ASSIGNEE(S): (MIRU-N) MIRUS CORP; (BUDK-I) BUDKER V G; (KNEC-I) KNECHTLE S J; (WOLF-I) WOLFF J A
COUNTRY COUNT: 21
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9955379	A1	19991104	(200005)*	EN	64 <--

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: JP
EP 1075283 A1 20010214 (200111) EN
R: AT BE CH CY DE DK ES FR GB IE IT LI NL SE
US 2001009904 A1 20010726 (200146)
JP 2002512985 W 20020508 (200234) 70

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9955379	A1	WO 1999-US8966	19990423
EP 1075283	A1	EP 1999-918823	19990423
		WO 1999-US8966	19990423
US 2001009904	A1 CIP of	US 1997-533	19971230
		US 1998-70303	19980430
JP 2002512985	W	WO 1999-US8966	19990423
		JP 2000-545576	19990423

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1075283	A1 Based on	WO 9955379
JP 2002512985	W Based on	WO 9955379

PRIORITY APPLN. INFO: US 1998-70303 19980430; US 1997-533 19971230
AN 2000-062007 [05] WPIDS
AB WO 9955379 A UPAB: 20000128
NOVELTY - ***Polynucleotides*** are delivered into ***parenchymal*** cells in vivo or ex vivo by ***transfecting*** the cells with ***polynucleotides*** delivered intravascularly.
USE - The method is useful to transfer ***polynucleotides*** into mammalian (especially human) ***parenchymal*** cells in vivo or ex vivo (e.g. for later transplantation). It is useful therapeutically to produce cellular changes (i.e. in gene therapy) e.g. to cause the expression of foreign genes in tissues, especially the liver. For example, a ***polynucleotide*** expressing the protein dystrophin, which is missing or defective in Duchenne muscular dystrophy, can be delivered to selected cells enabling dystrophin production from formerly deficient cells. The ***polynucleotides*** may also be ***polynucleotides*** which bind with ***RNA*** , ***DNA*** , ***nucleic*** ***acid*** hybrids, derivatives of natural nucleotides or protein to produce a therapeutic effect, e.g. natural/synthetic ***polynucleotides*** which prevent expression such as antisense ***polynucleotides*** (claimed). They may also be ***polynucleotides*** recombining with ***RNA*** , ***DNA*** , ***nucleic*** ***acid*** hybrids, derivatives of natural nucleotides or protein (claimed) e.g. to change the sequence of a gene for therapeutic purposes.
ADVANTAGE - An intravascular route of administration enables the

polynucleotide to be delivered to the ***parenchymal*** cells more evenly and more efficiently than prior art direct ***parenchymal*** injections. For example, delivery of naked ***DNA*** into the portal ***vein*** of the liver lobes of mice was more than an order of magnitude more efficient than direct injection by published methods and gave a more even distribution. Increasing the permeability of the tissue's ***blood*** ***vessel*** in the preferred method was also demonstrated to further increase the efficiency of ***polynucleotide*** delivery and expression.
Dwg.0/6

L10 ANSWER 25 OF 31 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1999-527254 [44] WPIDS
DOC. NO. NON-CPI: N1999-390560
DOC. NO. CPI: C1999-154823
TITLE: Increasing amounts of regulatory proteins in tissue constructs through cryopreservation and thawing, useful for wound healing and repair and regeneration of other tissue defects.
DERWENT CLASS: A32 A96 A97 B04 D16 P34
INVENTOR(S): LIU, K; MANSBRIDGE, J N
PATENT ASSIGNEE(S): (ADTI-N) ADVANCED TISSUE SCI INC
COUNTRY COUNT: 84
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9938952	A2	19990805 (199944)*	EN	68	<--

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD
GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV
MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT
UA UG US UZ VN YU ZW

AU 9925695	A	19990816 (200002)	<--
US 6291240	B1	20010918 (200157)	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9938952	A2	WO 1999-US2006	19990129
AU 9925695	A	AU 1999-25695	19990129
US 6291240	B1 Provisional	US 1998-72945P	19980129
		US 1998-137567	19980821

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9925695	A Based on	WO 9938952

PRIORITY APPLN. INFO: US 1998-137567 19980821; US 1998-72945P 19980129
AN 1999-527254 [44] WPIDS
AB WO 9938952 A UPAB: 19991026
NOVELTY - Subjecting a tissue construct to cryopreservation and subsequent thawing to increase the amount of regulatory proteins is new.
DETAILED DESCRIPTION - A tissue construct prepared in vitro comprising cells attached to a substrate, subjected to cryopreservation and subsequent thawing has an increased amount of at least one regulatory protein relative to constructs that are not subjected to cryopreservation and thawing.
INDEPENDENT CLAIMS are also included for the following:
(1) a three-dimensional (3-D) tissue construct prepared in vitro comprising a living stromal matrix comprising stromal cells and connective tissue proteins naturally secreted by the stromal cells attached to and enveloping a framework composed of a biocompatible, non-living material formed into a 3-D structure, having been subjected to cryopreservation and subsequent thawing has an increased amount of at least one regulatory protein relative to constructs that are not subjected to cryopreservation and thawing;
(2) inducing the production of at least one regulatory protein in cells in vitro, especially on a 3-D tissue construct; and
(3) methods for culturing ***parenchymal*** cells in vitro.
ACTIVITY - Vulnerary; Proliferative; Differentiation.
MECHANISM OF ACTION - Tissue Implant.
USE - The tissue constructs, especially 3-D constructs, are useful for implantation in vivo. The constructs are used to promote wound healing and to promote repair or regeneration of tissue damage, of e.g. skin, cartilage, bone and ***vascular*** tissue. The constructs and methods can also be used to enhance the culture and/or differentiation of cells and tissue in vitro. All claimed.
DESCRIPTION OF DRAWING(S) - Induction of PDGF A chain mRNA expression in 3-D dermal tissue constructs after cryopreservation and thawing relative to levels in fresh non-cryopreserved, tissue constructs.
Dwg.1/15

L10 ANSWER 26 OF 31 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1999-105547 [09] WPIDS
DOC. NO. CPI: C1999-031389
TITLE: Delivering a ***polynucleotide*** to ***parenchyma*** via the ***vascular*** system - comprises transporting the ***polynucleotide*** into a vessel communicating with the cell, useful for gene therapy of liver.
DERWENT CLASS: B04 D16
INVENTOR(S): BUDKER, V; KNECHTLE, S J; WOLFF, J A
PATENT ASSIGNEE(S): (MIRU-N) MIRUS CORP; (MIRU-N) MIRUS INC
COUNTRY COUNT: 18
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9858542	A1	19981230 (199909)*	EN	38	<--

RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE

EP 996337	A1	20000503 (200026)	EN

R: AT BE CH DE DK ES FR GB IE IT LI NL SE

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9858542	A1	WO 1997-US10767	19970620
EP 996337	A1	EP 1997-931309	19970620
		WO 1997-US10767	19970620

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 996337	A1 Based on	WO 9858542

PRIORITY APPLN. INFO: WO 1997-US10767 19970620
AN 1999-105547 [09] WPIDS
AB WO 9858542 A UPAB: 19990302
A new process for delivering a ***polynucleotide*** into a mammal ***parenchyma*** cell, comprises transporting the ***polynucleotide*** into a vessel communicating with that cell, so that the ***polynucleotide*** is ***transfected*** into the cell.
USE - The process is useful for gene therapy of the mammalian liver (disclosed).
ADVANTAGE - Intravascular delivery allows more even distribution and more efficient expression of ***polynucleotides*** than direct delivery to ***parenchymal*** cells
Dwg.0/7

L10 ANSWER 27 OF 31 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1998-457109 [39] WPIDS
CROSS REFERENCE: 2000-224554 [19]; 2001-366486 [38]; 2001-464214 [50]
DOC. NO. CPI: C1998-138274
TITLE: Gene therapy vectors for ***transfecting*** smooth muscle cells - useful in treatment of erectile dysfunction.

DERWENT CLASS: B04 D16
INVENTOR(S): CHRIST, G J; GELIEBTER, J; MELMAN, A; REHMAN, J
PATENT ASSIGNEE(S): (YESH) UNIV YESHIVA EINSTEIN COLLEGE
COUNTRY COUNT: 82
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9836055	A1	19980820 (199839)*		EN	43 <--
RW: AT BE CH DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW					
AU 9861468	A	19980908 (199904)			<--
EP 1005538	A1	20000607 (200032)		EN	
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
US 6150338	A	20001121 (200101)			
KR 2000071061	A	20001125 (200131)			
JP 2001517935	W	20011009 (200174)			42
AU 745637	B	20020328 (200235)			

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9836055	A1	WO 1998-US2249	19980205
AU 9861468	A	AU 1998-61468	19980205
EP 1005538	A1	EP 1998-906170	19980205
		WO 1998-US2249	19980205
US 6150338	A	US 1997-799144	19970213
KR 2000071061	A	WO 1998-US2249	19980205
		KR 1999-707330	19990813
JP 2001517935	W	JP 1998-535822	19980205
		WO 1998-US2249	19980205
AU 745637	B	AU 1998-61468	19980205

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9861468	A Based on	WO 9836055
EP 1005538	A1 Based on	WO 9836055
KR 2000071061	A Based on	WO 9836055
JP 2001517935	W Based on	WO 9836055
AU 745637	B Previous Publ.	AU 9861468
	Based on	WO 9836055

PRIORITY APPLN. INFO: US 1997-799144 19970213
AN 1998-457109 [39] WPIDS
CR 2000-224554 [19]; 2001-366486 [38]; 2001-464214 [50]
AB WO 9836055 A UPAB: 20011217
Genes are transferred into smooth muscle cells (SMC) by introducing a ***DNA*** sequence (I) that encodes a protein (II) involved in regulation of smooth muscle tone. Also new are: (1) recombinant vector containing (I) linked to ***DNA*** of, or corresponding to, at least part of a viral genome and able to direct expression of (I); and (2) SMCs expressing at least one (I).

USE - (II) modulate vasoconstriction or vasorelaxation and the method is used to treat penile erectile dysfunction where caused by incomplete relaxation of smooth muscle or by neurogenic, arteriogenic or veno-occlusive dysfunction.

ADVANTAGE - Only a relatively small proportion of corporal SMC need to be modified and injected (I) is retained largely in the corporal ***parenchyma*** so that any risks of systemic ***vascular*** side effects are low. The effect may persist for months.

Dwg.0/5

L10 ANSWER 28 OF 31 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:546093 HCAPLUS
DOCUMENT NUMBER: 135:117911
TITLE: Process of delivering a ***polynucleotide*** to a cell via the ***vascular*** system
INVENTOR(S): Wolff, Jon A.; Knechtle, Stuart J.; Budker, Vladimir G.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 27 pp., Cont.-in-part of U.S. Ser. No. 533.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2001009904	A1	20010726	US 1998-70303	19980430
US 2002001574	A1	20020103	US 1997-533	19971230
WO 9955379	A1	19991104	WO 1999-US8966	19990423 <--
W: JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1075283	A1	20010214	EP 1999-918823	19990423
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE, IE				
JP 2002512985	T2	20020508	JP 2000-545576	19990423

PRIORITY APPLN. INFO.: US 1995-571536 A 19951213
US 1997-533 A2 19971230
US 1998-70303 A 19980430
WO 1999-US8966 W 19990423

AB The present invention provides for the transfer of ***polynucleotides*** into ***parenchymal*** cells within tissues in situ and in vivo. An intravascular route of administration enables a prepd. ***polynucleotide*** to be delivered to the ***parenchymal*** cells more evenly distributed and more efficiently expressed than direct ***parenchymal*** injections. The efficiency of ***polynucleotide*** delivery and expression was increased substantially by increasing the permeability of the tissue's ***blood*** ***vessel*** . This was done by increasing the intravascular hydrostatic (phys.) pressure and/or increasing the osmotic pressure. Expression of a foreign ***DNA*** was obtained in mammalian liver by intraportally injecting ***plasmid*** ***DNA*** in a hypertonic soln. and transiently clamping the hepatic ***vein*** /inferior vena cava. Optimal expression was obtained by clamping the portal ***vein*** and injecting the hepatic ***vein*** /inferior vena cava.

L10 ANSWER 29 OF 31 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:300598 HCAPLUS
DOCUMENT NUMBER: 127:195
TITLE: Kidney-targeted liposome-mediated gene transfer in mice
AUTHOR(S): Lai, L.-W.; Moeckel, G. W.; Lien, Y.-H. H.
CORPORATE SOURCE: Dep. Pediatrics, Section Medical and Molecular Genetics, Univ. Arizona Health Sciences Center, Tucson, AZ, 85724, USA
SOURCE: Gene Therapy (***1997***), 4(5), 426-431
CODEN: GETHEC; ISSN: 0969-7128
PUBLISHER: Stockton
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To develop gene therapy targeted to the kidney, the authors compared three different routes of liposome-mediated gene delivery to the kidney in mice, i.e. intra-renal-pelvic, intra-renal-arterial, and intra-renal-***parenchymal*** injections. A ***plasmid*** construct, pCMV.beta.gal, contg. a cytomegalo-virus (CMV) immediate-early gene promoter and a .beta.-galactosidase reporter gene was mixed with a 1:1 liposome mixt. of N[1-(2,3-dioleoyloxy)propyl]-N,N,trimethylammonium chloride (DOTMA)/dioleoyl phosphatidyl ethanolamine (DOPE). The pCMV.beta.gal-liposome complex was injected into the kidney via three different routes. The efficacy of gene transfer was assessed using 5-bromo-4-chloro-3-indolyl .beta.-D-galactopyranoside (X-gal) staining on frozen kidney sections 3 to 42 days after injections. Cells with .beta.-galactosidase activity were detected in the cortex and outer

medulla in both intra-renal-pelvic and intra-renal-arterial groups, but not in the intra-renal- ***parenchymal*** group or in the contralateral noninjected kidney. Evidence of gene transfer was obsd. only in tubular epithelial cells, but not in glomerular, ***vascular*** , or interstitial compartments. The levels of .beta.-galactosidase expression started to decrease 3 wk after injection. The gene transfer in the kidney was not assocd. with nephrotoxicity as assessed by blood urea nitrogen levels and renal histol. The authors conclude that both intra-renal-pelvic and intra-renal-arterial injections provide a transient gene transfer to the renal tubular cells and are suitable routes for kidney targeted gene therapy.

L10 ANSWER 30 OF 31 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:198531 HCAPLUS
DOCUMENT NUMBER: 124:298491
TITLE: Receptor-mediated gene transfer to hepatic cells using asialofetuin-labeled liposomes
AUTHOR(S): Tsuchiya, Seishi; Hara, Toshifumi
CORPORATE SOURCE: Sch. Pharm., Tokyo Univ. Pharm. Life Sci., Hachioji, 192-03, Japan
SOURCE: Drug Delivery Syst. (***1996***), 11(1), 11-20
CODEN: DDSYEI; ISSN: 0913-5006
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review, with 36 refs. Asialofetuin-labeled liposomes (AF-liposomes) have been developed as an advantageous vector for asialoglycoprotein receptor (AgpR)-mediated gene transfer to hepatic cells. ***Plasmid*** pSV2CAT ***DNA*** which encoded bacterial chloramphenicol acetyltransferase (CAT) was almost completely assocd. to AF-liposomes (AF-liposome-pSV2CAT) contg. N-(.alpha.-trimethylamino-acetyl)-didodecyl-D-glutamate chloride (TMAG), and approx. two-thirds of the assocd. ***DNA*** was encapsulated in the internal phase. AF-liposome-pSV2CAT was efficiently incorporated into the cultured human hepatoblastoma cell line, HepG2, by the RME and significantly high CAT activity was expressed in the cells. The cat activity in A431 and Swiss/3T3 cells ***transfected*** with AF-liposome-pSV2CAT was low and almost the same as those ***transfected*** by pSV2CAT assocd. with non-labeled control liposomes. After injection of AF-liposome-pSV2CAT into a portal of femoral ***vein*** of BALB/c mice, CAT activity was expressed specifically in the liver. Immunohistochem. staining revealed that the CAT was developed in a large no. of ***parenchymal*** cells localized in the periportal area. Pretreatment of the cells or animals with EDTA-encapsulated AF-liposomes increased the gene expression efficiency of AF-liposome-pSV2CAT in vitro and in vivo. AF-liposomes are capable of protecting the encapsulated ***plasmid*** DNAs from environmental degrdn. in circulating blood and targeting them into hepatocytes by way of AgpR.

L10 ANSWER 31 OF 31 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:33688 HCAPLUS
DOCUMENT NUMBER: 118:33688
TITLE: Cationic lipid-mediated ***transfection*** of liver cells in primary culture
AUTHOR(S): Jarnagin, William R.; Debs, Robert J.; Wang, Shao Shean; Bissell, D. Montgomery
CORPORATE SOURCE: Univ. California, San Francisco, CA, 94110, USA
SOURCE: Nucleic Acids Res. (***1992***), 20(16), 4205-11
CODEN: NARHAD; ISSN: 0305-1048
DOCUMENT TYPE: Journal
LANGUAGE: English
AB ***Transfection*** of ***DNA*** into ***parenchymal*** and individual non- ***parenchymal*** cell populations from adult rat liver in early primary culture, using cationic lipid as the carrier, is described. All cell populations were ***transfectable*** , although lipid requirements varied by cell type and, for hepatocytes, with the age of the culture. For hepatocytes in early primary culture (2-10 h after plating), pure DOTMA (N-[1-(2,3-dioleyloxy)propyl]-N,N,N-trimethylammonium chloride) was strikingly more effective than com. formulations (Lipofectin or ***TransfectACE***) contg. components in addn. to, or other than DOTMA. For hepatocytes fully adapted to culture (.apprx.48 h after plating), pure DOTMA and Lipofectin were similarly effective. Under optimal conditions, about 10% of hepatocytes expressed the ***transfected*** reporter gene. CAT expression in hepatocytes doubled from 48 h to 7 days after ***transfection*** . The effect of culture substratum on ***transfection*** efficiency also was examd. The presence of basement membrane-like matrix (EHS gel) reduced uptake of the ***DNA*** -lipid complex. However, cells in early culture that were ***transfected*** on collagen and then replated on EHS gel, displayed significantly greater reporter gene activity than did cells maintained throughout on collagen. In contrast to hepatocytes, non-***parenchymal*** cells (lipocytes, Kupffer cells and endothelial cells, resp.) were ***transfected*** most efficiently by Lipofectin; DOTMA alone was inactive. The methods described will facilitate studies of gene regulation in individual liver cell populations.